REMARKS

I. INTRODUCTION

Receipt of the Office Action of October 28, 2002 is acknowledged. The undersigned appreciates the acknowledgement that claims 48, 101 and 104 are free of the prior art. Claims 1-47, 49-100, 102-103 and 105 are canceled without prejudice or disclaimer. The cancellation of claims does not constitute acquiescence to the propriety of any rejection of objection set forth by the Examiner. Applicants reserve the right to file one or more divisional applications directed to the canceled subject matter.

After amending the claims as set forth above, claims 48, 101 and 104 are now pending in this application.

II. THE OFFICE ACTION

A. Election/Restriction

The Examiner has maintained the restriction of the claims and has cited to numerous references which allegedly teach sPLA2 inhibitors. Without acquiescing to the position of the Examiner, non-elected claims have been canceled.

B. Drawings

The Examiner has directed Applicant's attention to the PTO-948 from the Draftsperson with changes to be made to the drawings. With the present response, Applicants submit formal drawings for consideration by the Examiner.

C. Claim Objections

The Examiner has objected to claim 46 as a substantial duplicate of claim 38. Applicants respectfully traverse the objection. Without acquiescing to the position of the Examiner, claims 46 and 38 have been canceled without prejudice or disclaimer. However, the Examiner's attention is directed to the language of claims 46 and 38 which state respectively:

38. A method of preventing ischemia reperfusion injury, which comprises administration of an $sPLA_2$ inhibitor **before** reperfusion of blood to an organ which is in an ischemic condition caused by surgery or cardiac standstill.

46. A method of preventing ischemia reperfusion injury, which comprises administration of an $sPLA_2$ inhibitor **after** reperfusion of blood to an organ which is in an ischemic condition caused by surgery or cardiac standstill.

The claimed methods are directed to administration of an sPLA2 inhibitor at different times following reperfusion of blood to an organ.

However, due to cancellation of the claims, the objection is moot.

D. Rejections based on 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 35-49, 57, 101 and 104 under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants respectfully traverse the rejection. Without acquiescing to the position of the Examiner, claims 35-47, 48 and 57 have been canceled without prejudice or disclaimer. It is understood that claims 48, 101 and 104 were included in the rejection because claims 48, 101 and 104 are dependent claims based on rejected independent claims. Due to cancellation of claims 37, 44 and 45, the rejection is moot.

E. Rejections based on 35 U.S.C. § 102(b)

The Examiner has rejected claims 35-40, 42-47 and 49 under 35 U.S.C. § 102(b) as allegedly anticipated by Sonnino. Applicants respectfully traverse the rejection. Without acquiescing to the position of the Examiner, claims 35-40, 42-47 and 49 have been canceled without prejudice or disclaimer.

The Examiner has rejected claim 41 under 35 U.S.C. § 102(b) as allegedly anticipated by Khau. Applicants respectfully traverse the rejection. Without acquiescing to the position of the Examiner, claim 41 has been canceled without prejudice or disclaimer.

F. Rejections based on 35 U.S.C. § 103(a)

The Examiner has rejected claims45under 35 U.S.C. § 103(a) as allegedly unpatentable over Sonnino. Applicants respectfully traverse the rejection. Without acquiescing to the position of the Examiner, claim 45 has been canceled without prejudice or disclaimer.

III. CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date March 28, 2003

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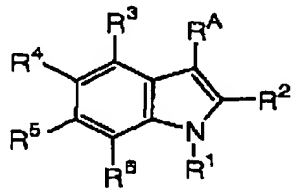
Should additional fees be necessary in connection with the filing of this paper, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees.

MARKED UP VERSION SHOWING CHANGES MADE

Below are the marked up amended claim(s):

48. (Amended) A method for treating ischemia reperfusion injury ~~of claim 43~~ which comprises administering to a subject an $sPLA_2$ inhibitor, wherein the $sPLA_2$ inhibitor ~~is a compound which contains~~ comprises a compound as an active ingredient, which is represented by the formula (I):



(I)

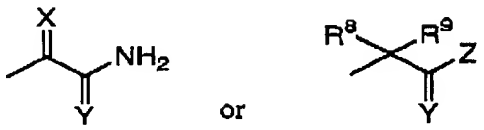
wherein R^1 is a group selected from (a) C7 to C20 alkyl, C7 to C20 alkenyl, C7 to C20 alkynyl, carbocyclic groups, and heterocyclic groups, (b) the groups represented by (a) each substituted independently with at least one group selected from non-interfering substituents, and (c) $-(L^1)-R^7$ wherein L^1 is a divalent linking group of 1 to 18 atom(s) selected from hydrogen atom(s), nitrogen atom(s), carbon atom(s), oxygen atom(s), and sulfur atom(s), wherein the combination atoms in L^1 are selected from the group consisting of i) carbon and hydrogen only, ii) sulfur only, iii) oxygen only, iv) nitrogen and hydrogen only, v) carbon, hydrogen, and sulfur only, and vi) carbon, hydrogen, and oxygen only and R^7 is a group selected from the groups (a) and (b);

R^2 is hydrogen atom, halogen, C1 to C3 alkyl, C3 to C4 cycloalkyl, C3 to C4 cycloalkenyl, C1 to C3 alkyloxy, or C1 to C3 alkylthio;

R^3 and R^4 are each independently hydrogen atom, non-interfering substituents, or $-(L^2)-$(acidic group) wherein L^2 is an acid linker having an acid linker length of 1 to 5, provided that one of R^3 and R^4 is $-(L^2)-$(acidic group);

R^5 and R^6 are each independently hydrogen atom, non-interfering substituents, carbocyclic groups, carbocyclic groups substituted with a non-interfering substituent(s), heterocyclic groups, or heterocyclic groups substituted with a non-interfering substituent(s); and

R^A is a group represented by the formula:



wherein R^8 and R^9 are each independently hydrogen atom, C1 to C3 alkyl or halogen; X and Y are each independently oxygen atom or sulfur atom; and Z is $-NH_2$ or -

$NHNH_2$;

the prodrugs thereof; their pharmaceutically acceptable salts; or their hydrates.

101. (Amended) A method of ~~claim 57~~ treating or preventing ischemia reperfusion injury, which comprises administering to a subject an $sPLA_2$ inhibitor, wherein the $sPLA_2$ inhibitor is selected from the group consisting of:

[3-(2-amino-1,2-dioxoethyl)-2-methyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid, dl-2-[[3-(2-amino-1,2-dioxoethyl)-2-methyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]propanoic acid,

[[3-(2amino-1,2-dioxoethyl)-1-([1,1'-biphenyl]-2-yl-methyl)-2-methyl-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-1-([1,1'-biphenyl]-3-yl-methyl)-2-methyl-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-1-([1,1'-biphenyl]-4-yl-methyl)-2-methyl-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxethyl)-1-[(2,6-dichlorophenyl)methyl]-2-methyl-1H-indole-4-yl]oxy]acetic acid,

[[3-2-amino-1,2-dioxoethyl)-1-[(4-fluorophenyl)methyl]-2-methyl-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-2-methyl-1-[(1-naphthyl)methyl]-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-2-ethyl-6-methyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-6-carboxy-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-1-[(3-chlorophenyl)methyl]-2-ethyl-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxethyl)-1-([1,1'-bipheny]-2-yl-methyl)-2-ethyl-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-1-([1,1'-biphenyl]-2-yl-methyl)-2-propyl-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-2-cyclopropyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid,

[[3-(2-amino-1,2-dioxoethyl)-1-([1,1'-biphenyl]-2-yl-methyl)-2-cyclopropyl-1H-indole-4-yl]oxy]acetic acid,

4-[[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-5-yl]oxy]butanoic acid,

~~2-[[1-(2-amino-1,2-dioxoethyl)-2-ethyl-3-phenylmethyl-indolizine-8-yl]oxy]acetic acid,~~

~~2-[[1-(2-amino-1,2-dioxoethyl)-3-(2-biphenyl)methyl-2-ethylinzolizine-8-yl]oxy]acetic acid,~~

~~2-[[1-(2-amino-1,2-dioxoethyl)-3-(2-biphenyl)methyl-2-cyclopropylindolizine-8-yl]oxy]acetic acid,~~

~~2-[[3-(2-amino-2-oxoethyl)-2-ethyl-1-phenylmethylene-1H-indene-4-yl]oxy]acetic acid,~~

~~2-[[3-(2-amino-2-oxoethyl)-2-ethyl-1-(1-naphthyl)methylene-1H-indene-4-yl]oxy]acetic acid,~~

~~2-[[8-(2-amino-1,2-dioxoethyl)-7-ethyl-3-methyl-6-phenylmethyl-[1,2-a]pyrazine-1-yl]oxy]acetic acid,~~

~~2-[[8-(2-amino-1,2-dioxoethyl)-7-ethyl-3-methyl-6-(2-biphenyl)methyl-[1,2-a]pyrazine-1-yl]oxy]acetic acid,~~

~~2-[[8-(2-amino-1,2-dioxoethyl)-6-cyclopropylmethyl-7-ethyl-3-methyl-[1,2-a]pyrazine-1-yl]oxy]acetic acid,~~

~~2-[[8-(2-amino-1,2-dioxoethyl)-7-ethyl-3-phenyl-6-phenylmethyl-[1,2-a]pyrazine-1-yl]oxy]acetic acid,~~

~~2-[[5-(2-amino-1,2-dioxoethyl)-6-ethyl-7-phenylmethyl-[1,2-b]pyridazine-4-yl]oxy]acetic acid,~~

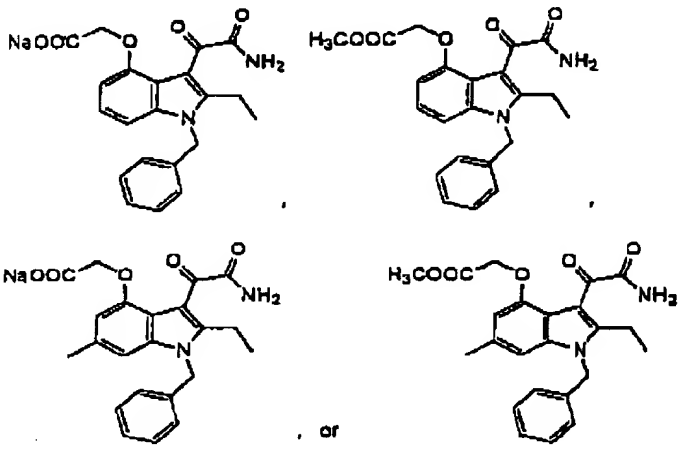
~~2-[[5-(2-amino-1,2-dioxoethyl)-2,6-dimethyl-7-phenylmethyl-[1,2-b]pyridazine-4-yl]oxy]acetic acid,~~

~~2-[[5-(2-amino-1,2-dioxoethyl)-6-ethyl-2-phenyl-7-phenylmethyl-[1,2-b]pyridazine-4-yl]oxy]acetic acid, and~~

~~(5-carbamoyl-9-cyclohexylmethyl-9H-carbazole-4-yl-oxy)acetic acid,~~

and the prodrugs thereof; their pharmaceutically acceptable salts; or their hydrates.

104. (Amended) ~~The~~ A method of ~~claim 57,~~ treating or preventing ischemia reperfusion injury, which comprises administering to a subject an $sPLA_2$ inhibitor, wherein the $sPLA_2$ inhibitor is one of the formulae:



, or

or their hydrates.